I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

axed to 703-305-3014

Attorney Docket No.: 15270-004300US Client Reference No.: 00188-US-NEW

Assistant Commissioner for Patents

Washington, D.C. 20231

On NOV. 25 2001

TOWNSEND and TOWNSEND and CREW LLP

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Examiner:

Philip Gambel

S. A. Rubin et al.

Art Unit:

1644

Application No.: 09/010,377 Filed: January 21, 1998

For: TREATMENT OF VIRAL

ENCEPHALITIS BY AGENTS

BLOCKING ALPHA-VLA-4 INTEGRIN FUNCTION

DECLARATION OF STEPHEN J. KARLIK

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

I, Stephen J. Karlik, state as follows:

- I, Stephen J. Karlik, am a Professor, University of Western Ontario, London, Ontario, Canada, and am an expert in the field of animal models for multiple sclerosis and other inflammatory disorders.
- I have reviewed the relevant portion of the subject patent application and the Office 2. Action dated July 31, 2000. The application has claims directed to methods of treating viral encephalitis in a patient free of multiple sclerosis using an agent that inhibits binding of leukocytes to brain endothelial cells via leukocyte surface antigen alpha-4 integrin. I

**PATENT** 

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understand that the Examiner has cited the following references in rejecting the claimed invention as allegedly being obvious: Bendig et al. (U.S. Patent No. 5,840,299), Soilu-Hanninen et al. (Scand. J. Immunol. 43: 727, 1996), and Soilu-Hanninen 1997 (J. Neuroimmunol. 72:95-105, 1997). I understand the Examiner has asserted that the models described in the cited references would have been predictive of the success of the presently claimed methods, and that the present claims are thus obvious in view of the cited references. Applicants have argued that these models would not have been predictive of the success of anti-VLA4 agents in treating viral encephalitis, as the animal models described in the cited references would not have been sufficiently predictive for the treatment of viral encephalitis in the absence of multiple sclerosis. My opinion is that the animal models discussed in the cited references are not predictive of the efficacy of anti-VLA4 agents in viral encephalitis in the absence of multiple sclerosis, that the animal model described in the present application specification is different from the models described in the cited references, and that the animal model of the application is predictive that agents to VLA-4 are useful in treating simple viral encephalitis. My opinion is based on the following facts.

3. The animal models discussed in the cited references show that antibodies to alpha-4 integrin are effective in inhibiting inflammation due to EAE, which is a syndrome simulating multiple sclerosis. However, multiple sclerosis is an autoimmune disease, and the inflammation present in EAE models results primarily, if not exclusively, from nonviral sources. For example, in Soilu-Hanninen's mice, EAE is induced by body irradiation and subsequent immunization with spinal cord homogenate; viral infection serves merely to augment the inflammatory response due to other factors. The avirulent Semliki virus alone does not induce encephalitis. The beneficial results from treatment with antibodies to alpha-4 integrin in Soilu-Hanninen's model may have been entirely or principally due to inhibition of inflammation resulting from the radiation and injection of brain homogenate rather than inhibition of inflammation resulting from viral infection. In the EAE model of Bendig et al., inflammation was due solely to irradiation and subsequence immunization, and thus the viral inflammation could not have been addressed in this model. Therefore, results from EAE models do not directly address the

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ability of antibodies to alpha-4 integrin to treat inflammation that is due exclusively to viral infection.

- 4. Inflammation that is solely due to viral infection presents great uncertainties for immunosuppressive treatment because of the complex role of inflammation clearing the virus and the resulting damage to surrounding tissues caused by such clearance. The combination of the beneficial and harmful consequences of viral infection-induced inflammation create uncertainty in the predictability of the immunosuppressive agents that would be useful in inhibiting such inflammation. For example, if treatment with an immunosuppressive agent increased the extent of viral infection as a result of decreased immune surveillance, the agent could effectively cause an increase in the damage to the subject. In fact, many immunosuppressive drugs currently prescribed by physicians have a warning label stating that immune suppression could increase susceptibility to infection.
- 5. The present application differs from the cited references in describing results from a model in which inflammation is solely the result of viral infection. Treatment with a4 integrin antibody was effective in preventing or ameliorating immune-mediated CNS damage following viral encephalitis in rats (see, e.g., pages 23-27). The effects included a reduction in prevalence and severity of clinical Borna disease, a reduction in body weight loss, and a reduction in the severity of encephalitis. Despite blocking the immunopathological immune response to viral encephalitis, the treatment did not cause enhanced viral replication (see, e.g., pages 27-28). These results indicate that treatment with antibodies to alpha-4 integrin is effective in suppressing the harmful effects of virally-induced inflammation without significantly suppressing the beneficial effects that keep viral replication in check.
- 6. In my opinion, this differential effect in suppressing harmful effects of inflammation without impairing beneficial effects resulting from treatment of simple viral infection with agents to alpha-4 integrin was not reasonably predictable from the animal models discussed in the references cited by the Examiner.

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**PATENT** 

7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date\_Nov 19, 2001

By Charlie

Stephen J. Karlik, Ph.D.

Attachments: curriculum vitae

### Stephen James Karlik Department of Diagnostic Radiology, 2MR21 London Health Sciences Centre

University Campus

339 Windermere Road London, Ontario, N6A 5A5

tel: 519-663-3648

fax: 519-663-3544 email: skarlik@irus.rri.on.ca

#### EDUCATION:

1969 Senior Matriculation, Assumption College School, Windsor

1972 BSc (Chemistry) McGill University, Montreal

1979 PhD (Physiology) University of Toronto, Toronto

Thesis Title: Aluminum Interactions with DNA and other Polynucleotides Supervisor: Dr. Donald R. Crapper-McLachlan

#### POST DOCTORAL:

1979-1983 Visiting Associate, Laboratory of Cellular and Molecular Biology, National Institutes of Health,

National Institute on Aging - Director: Dr. G.L. Eichhorn

#### ACADEMIC / EMPLOYMENT HISTORY:

#### PRIMARY APPOINTMENTS:

1983-1988 Assistant Professor, Department of Diagnostic Radiology and Nuclear Medicine, University of Western Ontario, London, Ontario

1988-1996 Associate Professor, Department of Diagnostic Radiology and Nuclear Medicine, University of Western Ontario, London, Ontario

1996-Present Professor, Department of Diagnostic Radiology and Nuclear Medicine, University of Western Ontario, London, Ontario

#### CROSS APPOINTMENTS:

1983-1989 Assistant Professor, Department of Clinical Neurological Sciences, University of Western Ontario London, Ontario

1987-Present Scientist, Imaging Research Laboratory, Robarts Research Institute, London, Ontario

1988-1996 Associate Professor, Department of Physiology, University of Western Ontario, London, Ontario 1988-Present

Honorary Lecturer, Department of Medical Biophysics, University of Western Ontario

Associate Professor, Department of Clinical Neurological Sciences, University of Western Ontario, 1989-1996 London, Ontario

1996-Present Professor, Department of Clinical Neurological Sciences, University of Western Ontario. London, Ontario

1996-Present Professor, Department of Physiology, University of Western Ontario, London, Ontario

1996-Present Honorary Lecturer, Department of Pathology, University of Western Ontario, London, Ontario

### CONTINUING EDUCATION:

### CONFERENCE AND PROFESSIONAL ANNUAL MEETING ATTENDANCE:

1977	Clinical Research Society of Toronto, Toronto Canadian Congress of Neurological Sciences
1979	Canadian Congress of Neurological Sciences XIth Internal Union of Biochemistry, Toronto American Chemical Society Gerontological Society
1981	American Society of Biological Chemistry Federation of American Society of Biological Chemists
1982	Canadian Chemical Congress American Chemical Society
1983	International Society of Magnetic Resonance Aluminum Analysis in Biological Materials
1984	Society of Magnetic Resonance in Medicine, New York American College of Neurology
1985	Canadian Association of Radiologists Rdiological Society of North America Society for Magnetic Resonance Imaging
1986	Canadian Congress of Neurological Sciences XII Symposium Neuroradiologicum Radiological Society of North America Metals, Aging and Alzheimer's Disease
1987	Canadian Association of Radiologists American Association of Physicists in Medicine Society of Magnetic Resonance in Medicine VI International Congress of Immunology
1988	Society of Magnetic Resonance in Medicine Society of Magnetic Resonance Imaging
1989	Society for Magnetic Resonance in Medicinc American Society for Neuroradiology Society for Magnetic Resonance Imaging American Academy of Neurology
1990	XIV Symposium Neuroradiologicum 76th Radiological Society of North America Society for Magnetic Resonance in Medicine
1991	Society of Magnetic Resonance in Medicine
1992	Society of Magnetic Resonance in Medicine Canadian Association of Radiologists 78th Radiological Society of North America

1993 XVII Canadian Congress of Neurological Sciences
Society of Magnetic Resonance in Medicine
79th Radiological Society of North America
Canadian Association of Radiologists

1994 IBC Cell Adhesion Meeting
Canadian Association of Radiologists
80th Radiological Society of North America
Society of Magnetic Resonance in Medicine

1995 Multiple Sclerosis Load Evaluation Workshop Society for Neuroscience Canadian Congress of Neurological Sciences Canadian Heads of Academic Radiology

1996 Asian Pacific Congress on Vascular Disease
1BC Cell Adhesion Molecules and Matrix Proteins
Radiological Society of North America
America's Committee for Treatment and Research in Multiple Sclerosis

Society for Experimental Neuropathology American Neurological Association Canadian Heads of Academic Radiology

1997 IBC Cell Adhesion Molecules
American Academy of Neurology

International Society for Magnetic Resonance in Medicine American Neurological Association International Society of Neuroimmunology Biology of Neurologic Disease Meeting Society for Health Services Research to Radiology

Society for Health Services Research in Radiology Canadian Heads of Academic Radiology

Canadian Heads of Academic Radiology European Society of Neuroradiology

Radiological Society of North America

2000 ECTRIMS RSNA

1998

1999

2001

1995

1996

ECTRIMS
ISMRM White Matter Study Group

ECTRIMS/ACTRIMS

#### FACULTY DEVELOPMENT:

Conflict Resolution and Confrontation Skills
Organizational Skills Workshop

HONOURS AND OTHER SPECIAL SCIENTIFIC RECOGNITION:

1978-1979 Studentship, Ontario Mental Health Foundation 1979-1982 Fogarty Fellowship, National Institutes of Health 1992-1994

Career Scientist, Sterling Winthrop Imaging Research Institute

### SCHOLARLY AND PROFESSIONAL ACTIVITIES:

### SOCIETY MEMBERSHIPS:

International Society of Magnetic Resonance in Medicine - ISMRM American Society of Neuroradiology - ASNR Radiological Society of North American - RSNA Canadian Association of Radiologists - CAR Society for Neuroscience -Society for Experimental Neuropathology Society for Health Services Research in Radiology

### NATIONAL SOCIETY EXECUTIVE:

Sccretary, 1993 -1998, Radiology Resident's Research Directors, CAR, CHAR Chairman, 1998-2000, Radiology Resident's Research Directors, CAR, CHAR

#### EDITORSHIP:

ACR - CAR Program in Fundamentals of Clinical Research for Radiologists (22 part series and web site)

## ROLES ON REVIEW BOARDS OF JOURNALS AND GRANTING AGENCIES:

#### 1. Ad Hoc Reviewer: Journal

<u>Journal</u>	Year(s)
Pharmachology	1985
Inorganic Chemica Acta	1985
Stroke	1985-present
Life Sciences	1987
Medical Physics	1987-present
Magnetic Resonance in Medicine	1989-present
Canadian Journal of Neurological Sciences	1990-present
Annals of Neurology	1990-present
Journal of Magnetic Resonance Imaging	1991-present
Canadian Veternary Journal	1992-present
Radiology	1997-present

#### Granting Agency

Medical Research Council of Canada	1985-present
Amyotrophic Lateral Sclerosis Society	1986
Gerontology Research Society of Ontario	1985
Ontario Mental Health Foundation	1987-present
Multiple Sclerosis Society of Canada	1989-present
Ottawa General Hospital Research Fund	1989
Winnipeg Health Sciences Center Research Foundation	1990-present
Sterling-Winthrop Imaging Research Institute	1992-93
Physicians Services Incorporated	1987-present

5

Fonds de la Recherche du Quebec Australian Research Council

1993-present 1995-present

#### 2.

Member of Study Section	
Study Section	Year(s)
Upjohn London Neurosciences Program	1989-91
National Institutes of Health -	1991-1992
National Institutes of Dental Research -	1999
Research Centres in Oral Biology Special Review Committee	.,,,,
Medical Research Council -	1993-present
Pharmaceutical Manufacturers Association of Canada -	1999 procent
University Industry	
Ontario Graduate Scholarships	1997-98
Multiple Sclerosis Society of Canada	2000-present

### VISITING PROFESSORSHIPS:

- 1) Grantmanship Workshop, McMaster University, 1991.
- 2) Grantmanship Workshop, University of Montreal, 1991.
- 3) Neurology, University of Aukland, New Zealand, 1996.
- 4) Radiology, Qucen's University, 2000.

#### SERVICE TO THE COMMUNITY:

Secretary/Treasurer, St. Mary's Home Support Services 1992 - 1998.

#### COMMITTEE MEMBERSHIPS:

#### DEPARTMENT:

- 1) 1993 - Present Resident Research Coordinator, Diagnostic Radiology and Nuclear Medicine, UWO.
- 2) 1993 - Present Residency Training Committee, Diagnostic Radiology and Nuclear Medicine, UWO
- 3) 1988 - Present Radiology Residents Research Director

#### HOSPITAL:

- 1. University Hospital: MRI Planning and Building Committee 1985-86.
- 2. University Hospital: MRI Phase II Planning and Building 1990-91.
- 3. University Hospital: Chairman, fMRI Planning Committee 1994-95.
- 4. London Health Sciences, University Campus: Chairman, MRI Upgrade Committee 1997-98.
- London Health Sciences: Executive, Scholars Forum 1996-1998.

### GRADUATE STUDENT AND RESEARCH TRAINEE SUPERVISION:

### Student Supervision

1.	Tom Stavraky	Msc	Physiology	1992	"Permeability Studies on the Blood-Brain Barrier"
2.	Sharon Hyduk	PhD	Physiology	1997	"a4 Integrin in Central Nervous System Inflammation" Recipient of MS Studentship
3.	Judy Karpecki	Msc	Physiology	1999	"Role of Metals in Integrin Adhesion"
4.	Matthew Erskinc	Msc	Physiology	1998	"MRI and MRS of MS Patients at 4T"
5.	Paula Piraino	PhD	Physiology	2003	"Prolonged anti & treatment in EAE" Recipient of OGSST
6.	Lisa Cook	PhD	Physiology	2003	"Advanced MRI Technologies in MS" Recipient of MS Studentship
7.	Shauna Kirk	MSc	Pathology	2002	"Mechanism of action of beta interferon"

### Medical Students 4th Year Elective Research

1.	John O'Brien (Oxford)	1989 - 90	"NMR Changes in EAE Precede Clinical and Pathological Events"
2	Daniel Struk	1997 - 93	"Stability Studies on Charman believe 1 (internet)"

### 4th Year Project Students

1.	Charlie Younger	1988 - 89	Chemistry (McMaster)	"Volumetric Determination of MS Plaques in MRI"
2,	Tamara Tram	1989 - 90	Electrical Engineering	"Acquiring EEG in High Field MRI"
3.	John Ieraci	1989 - 90	Electrical Engineering	"Digital Filtering for EEG Measurements in MRI"
4.	Tom Stavraky	1990 - 1 Phys	iology "Phosi	phorus NMR Spectroscopy in Epilepsy"
5.	Jeff Granton	1993 - 4 Phys		of Superoxide in Brain Inflammation"
6.	Roselyn Jeun	1992 - 3 Phys	4.5	sin Alters Clinical Progress of EAE"
7.	Eni Kesthelyi	1994 - 5 Phys		44 Treatment of Longstanding EAE"
8.	Jennifer Tondin	1995- 6 Phys	iology "Exten	ding Anti-a4 Therapy Using Tolerization"
9,	Paula Piraino	1996 - 7 Phys		tone Treatment of EAE"
				··· - · · · · · · · · · · · · · · · · ·

"Cell Trafficking and BBB Disruption"

### Radiology Residents, Research Project

Tomas Jimenez

1.	Leslie Vandenburgh	1992 - 93	"Chemoembolization mixtures" (Winner CAR Resident's Award)
2.	P.S. Olutola	1985 - 86	"Serum effects of radiographic contrast"

### **Advisory Committees**

10.

1.	Chao Zhong	MSc (Pharmacology)	1989 - 1991
2.	Eugene Florio	PhD (Biochemistry)	1989 - 1992
3.	Ross Mitchell	PhD (Biophysics)	1990 - 1996

1997 - 8 Physiology

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4.	Andrew Farrall	MSc (Biophysics)	1992 - 1995
5.	Scott Hamilton	PhD (Physiology)	1992 - 1996
6	Elizabeth Henderson	MSc (Biophyics)	1993 - 1999
7	Rob Bartha	MSc (Biophysics)	1994 - 1998
8	Joseph Gati	MSc (Biophysics)	1995 - 1996
9	Craig Jones	MSc (Biophysics)	1995 - 1997
10.	Constance Campbell	MSc (Biophysics)	1995 - 1997
11.	Chris Thomas	PhD (Biophysics)	1996 - 2000
12.	Jodi Adaıns	MSc (Physiology)	1997 - 2000
13.	Cheryl McCreary	PhD (Biophysics)	1998 - present
14.	Neil Duggal	MSc (Pathology)	1998 - 2001
15.	Angela Beye	MSc (Physiology)	1998 - present
16.	Eric Jensen	PhD (Biophysics)	1998 - present
17	Cameron Lush	PhD (Physiology)	1998 - 2001

## Post-doctoral Fellows:

1.	Eric Viiree	1992 - 1994	Dept. Of Otolaryngology and Human Interface Technology
			Laboratory
			University of Washington, Seattle
2.	Alan Taylor	1989 - 1990	Department of Chemistry
	·		University of Victoria, British Columbia
3.	Paula Gareau	1997 - 2000	Scientist, Imaging Laboratory, Robarts Research Institute
			Winner: Young Investigator Award ISMRM 2000

### Thesis Examiner

<u> </u>	SIB BARRING		
1.	Wendy Stewardt	PhD	University of British Columbia
2.	Joseph Maglesi	MSc	Biochemistry
3.	Ivan Yeung	PhD	Medical Biophysics
4.	Jeff Stanley	PhD	Medical Biophysics
5.	Cheryl McCreary MSc		Medical Biophysics
6.	Kathy Hamilton	PhD	Biochemistry
7.	Saryu Singh	PhD	Medical Biophysics
8.	Greet Peersman	PhD	Univ. of Antwerp
9.	Ian Callow	MSc	Pharmacology and Toxicology
10.	Raymond Chung	PhD	Physiology
11.	Susan Hochstenbach	PhD	Physiology
12.	Monica Way	MSc	Neuroscience
13.	Ramin Siushansian	PhD	Physiology
14.	John Potwarka	MSc	Medical Biophysics
15.	Cameron Lush	MSc	Physiology
16.	Jonas Vanderznan	MSc	Physiology
17	Rob Bartha	PhD	Medical Biophysics
18.	Lin Wang	MSc	McGill University
19.	Xi-Zhen Zhu	PhD	Chemistry
20.	Janine Robichaud	MSc	Microbiology and Immunology
21	L.Folev	PhD	Biochemistry, James Cook University

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#### CONTRIBUTIONS TO TEACHING AND EDUCATION:

### **Teaching**

1989 -	present	Biology 310 Laboratory	Cardiovascular and Respiratory	15 hrs. of 8)	Laboratory (groups	
1989 -	1998	Dental Physiology (415)	Respiratory System		Classroom (n=40)	
			Seminars	8 hrs.	Small Group	
1993 -	present	Critical Inquiry	Radiology Residents	24 hrs.	Small Group	
1990 -	present	Physiology 441y	Seminars	4 hrs.	Small Group	
1998 -	1998 - 2000 Oral Physiolog	Oral Physiology	Sensory Physiology 8 hrs		Classroom n=54	
		(Dentistry 115)	Seminars	8 hrs.	Small Groups	

#### RESEARCH FOCUS:

I am primarily interested in:

- The generation and evaluation of new therapies for multiple sclerosis.
- 2) The molecular basis of altered MRI/MRS in MS.

### RESEARCH FUNDING:

<u>Year</u> 1983	Grantor Academic Development, U.W.O.	<u>Investicators</u> Karlik	<u>Purpose</u> Start up	<u>Amount</u> 65,000
1984-85 Bant	ing Foundation	Karlik	MRI Research	18,700
1984-86 PSI		Noseworthy Karlik	EAE-NMR Studies	100,000
1987-92 MS S	Society	Karlik	EAE-MRI Studies	285,000
1987-89 Lede Labo	rle ratories	Karlik Noseworthy	Quantitation of Mitoxantrone treatment in EAE	30,000
1988-91 <b>Up</b> jo	hn Co.	Karlik	Lipid peroxidase inhibiters in BBB disease	147,000
1989 Upjo	hn Co.	Noseworthy Karlik	Quantitative MRI in MS	114,512
1986-90 MRC	:	Fox, Karlik	MRI of Dementia	117,000
1987-90 MRC	:	Feasby, Fox, Ebers, Karlik	Optic Neuritis	59,149

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1988-89 Henri & Stroke  Gelb, Karlik Drug Treatment in Stroke  1984-90 University Hospital Pooled Research Plund, University Hospital Foundation  Rarlik Noseworthy 1989-90 MS Society Rarlik Noseworthy 1991-94 Upjohn Co.  Karlik Lazaroid suppression of EAE  1992-93 Starling-Winthrop Imaging Research Institute  1992-94 Sterling-Winthrop Imaging Research Institute  1992-94 Sterling-Winthrop Imaging Research Institute  1992-94 Sterling-Winthrop Imaging Research Institute  1992-95 MS Society  Mitchell, Karlik, Automated Detection and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt  Karlik Quantifying Blood-Brain- Barrier Permiability Using MP 1177/10  1994-95 UH Pooled Research Fund  Downey, Karlik Intervention Chemical Carcinogens  1994-96 MS Society  Karlik, Rice An integrin-based therapy for Multiple Schrosis  1994-904 Athena Neurosciences/Elan  Karlik Cell Adhesion Studies in EAE  521,000  1996-97 Teva Pharmaceuticals  Karlik Anticytekine therapy in MS  210,000  MS Society  Karlik Anticytekine therapy in MS  21,000  1997-98 MS Society  Karlik, Rice MRI and MRS at 4T  33,000  1998-2000  MS Society  Fundamentals of Clinical Research for Radiologists  Fundamentals of Clinical Research for Radiologists			•		
Pooled Research Flund, University Hospital Foundation    1989-90 MS Society   Karlik   Quantitative MRI   110,000	1988-89 Heart &	Stroke	Gelb, Karlik		52,079
Noseworthy in MS  1991-94 Upjohn Co. Karlik Lazaroid suppression of EAE  1992-93 Sterling-Winthrop Imaging Research Institute  1992-94 Sterling-Winthrop Imaging Research Institute  1992-2002 MS Society  Mitchell, Karlik, Automated Detection and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt  Karlik Quantifying Blood-Brain-Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund  Downey, Karlik, Rice An integrin-based therapy for Multiple Sclerosis  1994-2004 Athera Neurosciences/Elan  Karlik Cell Adhesion Studies in EAE  521,000  1995-96 MS Society Hyduk Studentship (PhD Student)  1996-97 Teva Pharmaceuticals Karlik Anticytokine therapy in MS  1997-98 MS Society Karlik, Rice MRI and MRS at 4T  33,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T  33,000  1998-2000 MS Society Gareau PDF  50,000  1999-2002 OGSST  Piraino Studentship (Pund Research 450,000  for Radiologists	1984-90 Universi	Pooled Research Fund, University	Karlik	Grants (5) for	61,250
of EAE  1992-93 Sterling-Winthrop Imaging Research Institute  1992-94 Sterling-Winthrop Imaging Research Institute  1992-2002 MS Society  Mitchell, Karlik, Automated Detection and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt  Karlik  Career Scientist  420,000  As Society  Mitchell, Karlik, Automated Detection and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt  Karlik  Quantifying Blood-Brain-Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund  Downey, Karlik Intervention Chemical Carcinogens  1994-96 MS Society  Karlik, Rice  An integrin-based therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan  Karlik  Cell Adhesion Studies in EAE  521,000  1995-96 MS Society  Hyduk Studentship (PhD Student)  1996-97 Teva Pharmaceuticals  Karlik  Karlik  Anticytokine therapy in MS  21,000  1997-98 MS Society  Karlik, Rice  MRI and MRS at 4T  33,000  1998-2000  MS Society  Gareau  PDF  50,000  1999-2002  OGSST  Piraino  Studentship  Fundamentals of Clinical Research  450,000  for Radiologists	1989-90 MS Soci	ety		~	110,000
Irraging Research Institute  Irraging Research Institute  1992-94 Sterling-Winthrop Irraging Research Institute  1992-2002 MS Society  Mitchell, Karlik, Automated Detection and Quantification of MS lesions in MRI Irrages  1993-94 Mallinckrodt  Karlik Quantifying Blood-Brain-Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund  Downey, Karlik Intervention Chemical Carcinogens  1994-96 MS Society  Karlik, Rice An integrin-based therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan Karlik Cell Adhesion Studies in EAE 521,000  1995-96 MS Society Hyduk Studentship (PhD Student) 15,959 1996-97 Teva Pharmaceuticals Karlik Evaluation of Cop-1 25,000  1996-97 Biogen, Inc. Karlik Anticytokine therapy in MS 21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T 33,000  1998-2000 MS Society Gareau PDF 50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000	1991-94 Upjohn	Co.	Karlik		90,965
Imaging Research Institute  1992-2002 MS Society  Mitchell, Karlik, Automated Detection Lee, Rutt and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt  Karlik Quantifying Blood-Brain- Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund  Downcy, Karlik Intervention Chemical Carcinogens  Karlik, Rice An integrin-based therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan  Karlik Karlik Cell Adhesion Studies in EAE  521,000  1995-96 MS Society Hyduk Studentship (PhD Student) 15,959 1996-97 Teva Pharmaceuticals Karlik Karlik Anticytokine therapy in MS  21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T  33,000  1998-2000 MS Society Gareau PDF  50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000	1992-93 Sterling	Imaging Research	Karlik	oculomotor	14,423
Lee, Rutt and Quantification of MS lesions in MRI Images  1993-94 Mallinckrodt Karlik Quantifying Blood-Brain-Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund Downcy, Karlik Intervention Chemical Carcinogens  1994-96 MS Society Karlik, Rice An integrin-based therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan Karlik Cell Adhesion Studies in EAE 521,000  1995-96 MS Society Hyduk Studentship (PhD Student) 15,959 1996-97 Teva Pharmaceuticals Karlik Evaluation of Cop-1 25,000  1996-97 Biogen, Inc. Karlik Anticytokine therapy in MS 21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T 33,000  1998-2000 MS Society Gareau PDF 50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000  Reinhold, Fundamentals of Clinical Research 450,000	1992-94 Sterling		Karlik	Career Scientist	80,509
Barrier Permiability Using MP1177/10  1994-95 UH Pooled Research Fund  Downey, Karlik Intervention Chemical Carcinogens  1994-96 MS Society  Karlik, Rice An integrin-based therapy for Multiple Sclcrosis  1994-2004 Athena Neurosciences/Elan Karlik Cell Adhesion Studies in EAE 521,000  1995-96 MS Society Hyduk Studentship (PhD Student) 15,959 1996-97 Teva Pharmaceuticals Karlik Evaluation of Cop-1 25,000  1996-97 Biogen, Inc. Karlik Anticytokine therapy in MS 21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T 33,000  1998-2000 MS Society Gareau PDF 50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000 for Radiologists	1992-2002	MS Society		and Quantification of MS lesions in MRI	420,000
Carcinogens  1994-96 MS Society  Karlik, Rice An integrin-based therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan Karlik Cell Adhesion Studies in EAE 521,000  1995-96 MS Society Hyduk Karlik Evaluation of Cop-1 25,000  1996-97 Biogen, Inc. Karlik Anticytokine therapy in MS 21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T 33,000  1998-2000 MS Society Gareau PDF 50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000 for Radiologists	1993-94 Mallincl	scrodt	Karlik	Barrier Permiability	36,400
therapy for Multiple Sclerosis  1994-2004 Athena Neurosciences/Elan Karlik Cell Adhesion Studies in EAE 521,000  1995-96 MS Society Hyduk Studentship (PhD Student) 15,959 1996-97 Teva Pharmaceuticals Karlik Evaluation of Cop-1 25,000  1996-97 Biogen, Inc. Karlik Anticytokine therapy in MS 21,000  1997-98 MS Society Karlik, Rice MRI and MRS at 4T 33,000  1998-2000 MS Society Gareau PDF 50,000  1999-2002 OGSST Piraino Studentship 45,000  2000-2003 ACR Karlik, Fundamentals of Clinical Research 450,000 Beam, Fundamentals of Clinical Research 450,000 Beam,	1994-95 UH Pool	ed Research Fund	Downey, Karlik		6,500
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Reinhold, for Radiologists  Beam,	1999-2002	OGSST	Piraino	Studentship	45,000
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Cost of Angiography

2000-2001	CARROGINATION	Raine, Rainein	Cost of Anglography	20,000	
2000-2001	MS Society	Cook	Studentship	16,000	
2000-2001	Biogen	Karlik	Immunotherapy in MS	20,200	
2001-2004	CIHR	Karlik, Hammond	Remyelination in EAE	110,000	

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- 3. "NMR Studies in Alzheimer's Disease", McGill University, June 1982.
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- "Nuclear Magnetic Resonance Imaging Applications", Symposium, University of Western Ontario, March 1984. 9.
- "Factors Affecting NMR Imaging", National Institute of Health, June 1984.
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Updated 19/11/2001